

I hereby certify that this correspondence is being hand-delivered to:  
Examiner Teresa D. Wessendorf/ Examiner Andrew J. Wang  
United States Patent and Trademark Office  
Art Unit 1639  
1911 S. Clark Place  
Crystal Mall One, 7<sup>th</sup> Floor  
Arlington, VA 22202  
703-308-3967

On: October 8, 2003

By: Meredith K. Meyer

Printed Name: Meredith K. Meyer

Attorney Docket No. 0155.130US  
(formerly 18097-030310US)

RECEIVED  
OCT 9 11:04 PM  
10/9/2003

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

Juha Punnonen et al.

Application No.: 09/724,869

Filed: November 28, 2000

For: OPTIMIZATION OF  
IMMUNOMODULATORY  
PROPERTIES OF GENETIC  
VACCINES

Examiner: Teresa D. Wessendorf

Art Unit: 1639

#18  
10/9/03  
10-8-03

**SECOND SUPPLEMENTAL  
INFORMATION DISCLOSURE  
STATEMENT UNDER 37 CFR §§ 1.97  
AND 1.98**

Examiner Teresa D. Wessendorf  
Examiner Andrew J. Wang  
United States Patent and Trademark Office  
Art Unit 1639  
1911 S. Clark Place  
Crystal Mall One, 7<sup>th</sup> Floor  
Arlington, VA 22202

Dear Madam/Sir:

The references cited on attached form PTO/SB/08A-B are being called to the attention of the Examiner. Copies of the references are enclosed. It is respectfully requested that the cited information be expressly considered during the prosecution of this application and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no

10/09/2003 TSUGG  
01 FC:1806  
09/00001 505/90  
09/2486

Application No. 09/724,869

Page 2

representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

A Fee Transmittal Form is submitted concurrently herewith, authorizing the Commissioner to deduct any required fee from, or credit any overpayment to, the undersigned's Deposit Account No. 50-0990.

Respectfully submitted,

October 8, 2003

By: R. Danny Huntington  
**R. Danny Huntington**  
Registration No. 27,903  
**Sharon E. Crane**  
Registration No. 36,113  
**Mercedes K. Meyer**  
Registration No. 44,939  
**Attorneys for Applicants**

Maxygen, Inc.  
Patent Department  
515 Galveston Drive  
Redwood City, California 94063  
Telephone: (650) 298-5300  
Facsimile: (650) 298-5446  
Customer No. 30560

Substitute for form 1449A-B/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)	Complete if Known	
	Application Number	09/724,869
	Filing Date	November 28, 2000
	First Named Inventor	Juha Punnonen
	Group Art Unit	1639
	Examiner Name	Teresa Wessendorf
	Attorney Docket Number	0155.130US

U.S. PATENT DOCUMENTS						
Examiner Initials	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, lines, Where Relevant Passages or Relevant Figures Appeal
		Number	Kind Code (if known)			
	1	6,376,246		Crameri et al.	04-09-2002	

FOREIGN PATENT DOCUMENTS								
Exami ner Initials	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	
		Office	Number	Kind Code (if known)				
	2	WO	91/19818	A1	Affymax Technologies N.V.	12-26-1991		
	3	WO	92/01047	A1	Cambridge Antibody Technology Limited	01-23-1992		
	4	WO	92/18619	A1	The Scripps Research Institute	10-29-1992		
	5	WO	94/01567	A1	Unilever PLC	01-20-1994		
	6	WO	94/18330	A1	Unilever PLC	08-18-1994		

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Exami ner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	
	7	Aggarwal & Gutterman eds., HUMAN CYTOKINES: HANDBOOK FOR BASIC AND CLINICAL RESEARCH, Vol. II (1996) (Table of Contents for Vols. 1 & II)	
	8	Alcami <i>et al.</i> , "A soluble receptor for interleukin-1 beta encoded by vaccinia virus: a novel mechanism of virus modulation of the host response to infection," <i>Cell</i> 71(1):153-67 (1992)	
	9	Apostolopoulos <i>et al.</i> , "Breast cancer immunotherapy: Current status and future prospects," <i>Immunol. and Cell. Biol.</i> 74:457-64 (1996)	
	10	Atamas <i>et al.</i> , "An alternative splice variant of human IL-4, IL-4 delta 2, inhibits IL- 4-stimulated T cell proliferation," <i>J. Immunol.</i> 156(2):435-41 (1996)	
	11	Aversa <i>et al.</i> , "SLAM and its role in T cell activation and Th cell responses." <i>Immunol. Cell Biol.</i> 75(2):202-5 (1997)	
	12	Bach <i>et al.</i> , "The IFN gamma receptor: a paradigm for cytokine receptor signaling," <i>Annu. Rev. Immunol.</i> 15:563-91 (1997)	
	13	Baggioloni <i>et al.</i> , "Human Cytokines: An Update," <i>Annu. Rev. Immunol.</i> 15:675-705 (1997)	
	14	Balbas <i>et al.</i> , "Design and Construction of Expression Plasmid Vectors in Escherichia coli," in METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY 185:14-37 (David V. Goeddel ed., Acad. Press, Inc., 1990)	
	15	Basham <i>et al.</i> , "Synergistic antitumor activity with IFN and monoclonal anti-idiotype for murine B cell lymphoma. Mechanism of action," <i>J. Immunol.</i> 141(8):2855-60 (1988)	
	16	Beck <i>et al.</i> , "Analysis of Multiple Plasmodium falciparum Infections in Tanzanian Children during the Phase II Trial of Malaria Vaccine SPf66," <i>J. Inf. Disease</i> 175:921-26 (1997)	

17	Becket <i>et al.</i> , "Characterization of a Prostate Carcinoma Mucin-Like Antigen (PMA)," <i>Int. J. Cancer</i> 62:703-10 (1995)	
18	Bramson <i>et al.</i> , "Construction of a double recombinant adenovirus vector expressing a heterodimeric cytokine: in vitro and in vivo production of biologically active interleukin-12," <i>Hum. Gene Ther.</i> 7(3):333-42 (1996)	
19	Brusselle <i>et al.</i> , "Role of IFN- $\gamma$ in the Inhibition of Allergic Airway Inflammation Caused by IL-12," <i>Am. J. Respir. Cell Mol. Biol.</i> 17:767-71 (1997)	
20	Censini <i>et al.</i> , "cag, a pathogenicity island of <i>Helicobacter pylori</i> , encodes type I-specific and disease-associated virulence factors," <i>PNAS</i> 93:14648-53 (1996)	
21	Chen <i>et al.</i> , "Discontinuous epitopes of hepatitis B surface antigen derived from a filamentous phage peptide library," <i>PNAS USA</i> 93(5):1997-2001 (1996)	
22	Chow <i>et al.</i> , "Improvement of Hepatitis B Virus DNA Vaccines by Plasmids Coexpressing Hepatitis B Surface Antigen and Interleukin-2," <i>J. Virol.</i> 71(1):169-78 (1997)	
23	Ciernik <i>et al.</i> , "Induction of Cytotoxic T Lymphocytes and Antitumor Immunity with DNA Vaccines Expressing Single T Cell Epitopes," <i>J. Immunol.</i> 156:2369-75 (1996)	
24	Cohen <i>et al.</i> , "Host factors in the pathogenesis of HIV disease," <i>Immunol. Rev.</i> 159:31-48 (1997)	
25	Cortese <i>et al.</i> , "Selection of biologically active peptides by phage display of random peptide libraries," <i>Curr. Opin. Biotechnol.</i> 7(6):616-21 (1996)	
26	Curtis <i>et al.</i> , "Recombinant Soluble Interleukin-11 (IL-11) Receptor alpha Chain Can Act as an IL-11 Antagonist," <i>Blood</i> 90(11):4403-12 (1997)	
27	Cwirla <i>et al.</i> , "Peptide Agonist of the Thrombopoietin Receptor as Potent as the Natural Cytokine," <i>Science</i> 276:1696-9 (1997)	
28	Dagan <i>et al.</i> , "High level expression and production of recombinant human interleukin analogs," <i>Protein Expr. Purif.</i> 3(4):290-4 (1992)	
29	Devos <i>et al.</i> , "Interleukin-5 and its receptor: a drug target for eosinophilia associated with chronic allergic disease," <i>J. Leukoc. Biol.</i> 57(6):813-19 (1995)	
30	De Vries <i>et al.</i> , "Novel fundamental approaches to intervening in IgE-mediated allergic diseases," <i>J. Invest. Dermatol.</i> 102(2):141-4 (1994)	
31	De Vries <i>et al.</i> , <i>Interleukin-4 and Interleukin-13</i> , Chap. 8, in CYTOKINE REGULATION OF HUMORAL IMMUNITY: BASIC AND CLINICAL ASPECTS 195-215 (C. M. Snapper, West Sussex, UK, John Wiley and Sons, 1996)	
32	De Vries <i>et al.</i> , "Modulation of the human IgE response," <i>Eur. Respir. J. Suppl.</i> 22:58s-62s (1996)	
33	De Waal Malefyt <i>et al.</i> , "A Novel Cytokine Belonging to the IL-10 Gene Family Affects Human Monocytes and T Cells," Abstract, 13th European Immunology Meeting, Amsterdam, Netherlands, June 1997, <i>Immunol. Letters</i> 56(1):211 (May 1997)	
34	Donnelly <i>et al.</i> , "DNA Vaccines," <i>Annu. Rev. Immunol.</i> 15:617-48 (1997)	
35	Dudler <i>et al.</i> , "A Link Between Catalytic Activity, IgE-Independent Mast Cell Activation and Allergenicity of Bee Venom Phospholipase A <sub>2</sub> ," <i>J. Immunol.</i> 155(5):2605-13 (1995)	
36	Eckhart <i>et al.</i> , "Immunogenic presentation of a conserved gp41 epitope of human immunodeficiency virus type 1 on recombinant surface antigen of hepatitis B virus," <i>J. Gen. Virol.</i> 77 (9):2001-8 (1996)	
Examiner Signature		Date Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

37	Fomsgaard <i>et al.</i> , "Improved humoral and cellular immune response against the gp120 V3 loop of HIV-1 following genetic immunization with a chimeric DNA vaccine encoding the V3 inserted in the hepatitis B surface antigen," <i>Scand. J. Immunol.</i> 47(4):289-95 (1998)	
38	Foy <i>et al.</i> , "Immune regulation by CD40 and its ligand GP39," <i>Annu. Rev. Immunol.</i> 14:591-617 (1996)	
39	Fromm <i>et al.</i> , "Expression of genes transferred into monocot and dicot plant cells by electroporation," <i>PNAS USA</i> 82(17):5824-28 (1985)	
40	Gauchat <i>et al.</i> , "Regulation of human IgE synthesis: the role of CD4+ and CD8+ T-cells and the inhibitory effects of interferon-alpha," <i>Eur. Respir. J. Suppl.</i> 13:31s-38s (1991)	
41	Goff <i>et al.</i> , "Laboratory Methods: Efficient Saturation Mutagenesis of a Pentapeptide Coding Sequence Using Mixed Oligonucleotides," <i>DNA</i> 6(4):381-388 (1987)	
42	Greenfeder <i>et al.</i> , "Insertion of a Structural Domain of Interleukin (IL)-1B Confers Agonist Activity to the IL-1 Receptor Antagonist," <i>J. Biol. Chem.</i> 270:22460-6 (1995)	
43	Grewal <i>et al.</i> , "The CD40-CD154 system in anti-infective host defense," <i>Curr. Opin. Immunol.</i> 9(4):491-7 (1997)	
44	Grunig <i>et al.</i> , "Interleukin-10 is a natural suppressor of cytokine production and inflammation in a murine model of allergic bronchopulmonary aspergillosis," <i>J. Exp. Med.</i> 185(6):1089-99 (1997)	
45	Hannum <i>et al.</i> , "Interleukin-1 receptor antagonist activity of a human interleukin-1 inhibitor," <i>Nature</i> 343:336-40 (1990)	
46	Hathcock <i>et al.</i> , "Comparative Analysis of B7-1 and B7-2 Costimulatory Ligands: Expression and Function," <i>J. Exptl. Med.</i> 180:631-40 (1994)	
47	Herz <i>et al.</i> , "Molecular approaches to receptors as targets for drug discovery," <i>J. Recept. Signal Transduct. Res.</i> 17(5):671-776 (1997)	
48	Herzenberg <i>et al.</i> eds., WEIR'S HANDBOOK OF EXPERIMENTAL IMMUNOLOGY (5 <sup>th</sup> ed. 1996) (index and first pages of Chaps. 220, 226, 227)	
49	Hess <i>et al.</i> , "Superior efficacy of secreted over somatic antigen display in recombinant <i>Salmonella</i> vaccine induced protection against listeriosis," <i>PNAS</i> 93:1458-63 (1996)	
50	Hill <i>et al.</i> , "Mutagenesis with Degenerate Oligonucleotides: An Efficient Method for Saturating a Defined DNA Region with Base Pair Substitutions," in METHODS IN ENZYMOLOGY: RECOMBINANT DNA 155:558-568 (Ray Wu ed., Acad. Press, Inc., 1987)	
51	Horuk, "Molecular properties of the chemokine receptor family," <i>TIPS</i> 15:159-165 (1994)	
52	Horwitz <i>et al.</i> , "Saturation Mutagenesis Using Mixed Oligonucleotides and M13 Templates Containing Uracil," in METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY 185:599-611 (David V. Goeddel ed., Acad. Press, Inc. 1990)	
53	Ihle <i>et al.</i> , "Signaling through the hematopoietic cytokine receptors," <i>Annu. Rev. Immunol.</i> 13:369-98 (1995)	
54	Kaufman, "Vectors Used for Expression in Mammalian Cells," in METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY 185:487-511 (David V. Goeddel ed., Acad. Press, Inc., 1990)	
55	Kay <i>et al.</i> , eds., PHAGE DISPLAY OF PEPTIDES AND PROTEINS: A LABORATORY MANUAL (Acad. Press, Inc., 1996) (first page of Chap. 5)	
56	Krieger <i>et al.</i> , "Structures and functions of multiligand lipoprotein receptors: macrophage scavenger receptors and LDL receptor-related protein (LRP)," <i>Annu. Rev. Biochem.</i> 63:601-	
Examiner Signature		Date Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

	37 (1994)	
57	Kroemer <i>et al.</i> , "Immunoregulation by cytokines," <i>Crit. Rev. Immunol.</i> 13(2):163-91 (1993)	
58	Laberge <i>et al.</i> , "Secretion of IL-16 (Lymphocyte Chemoattractant Factor) from Serotonin-Stimulated CD8 <sup>+</sup> T Cells In Vivo," <i>J. Immunol.</i> 156(1):310-5 (1996)	
59	Le Borgne <i>et al.</i> , "In Vivo Induction of Specific Cytotoxic T Lymphocytes in Mice and Rhesus Macaques Immunized with DNA Vector Encoding an HIV Epitope Fused with Hepatitis B Surface Antigen," <i>Virology</i> 240:304-15 (1998)	
60	Le Grice, "Regulated Promoter for High-Level Expression of Heterologous Genes for <i>Bacillus subtilis</i> ," in METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY 185:201-15 (David V. Goeddel ed., Acad. Press, Inc., 1990)	
61	Levinson, "Expression of Heterologous Genes in Mammalian Cells," in METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY 185:485-87 (David V. Goeddel ed., Acad. Press, Inc., 1990)	
62	Livnah <i>et al.</i> , "Functional Mimicry of a Protein Hormone by a Peptide Agonist: The EPO Receptor Complex at 2.8," <i>Science</i> 273:464-71 (1996)	
63	Ma <i>et al.</i> , "Antibody production and engineering in plants," <i>Ann. NY Acad. Sci.</i> 792:72-81 (1996)	
64	Mattion <i>et al.</i> , "Characterization of recombinant polioviruses expressing regions of rotavirus VP4, hepatitis B surface antigen, and herpes simplex virus type 2 glycoprotein D," <i>J. Virol.</i> 69:5132-37 (1995)	
65	McLafferty <i>et al.</i> , "M13 bacteriophage displaying disulfide-constrained microproteins," <i>Gene</i> 128(1):29-36 (1993)	
66	Miele, "Plants as bioreactors for biopharmaceuticals: regulatory considerations," <i>Trends Biotechnol.</i> 15(2):45-50 (1997)	
67	Mosmann <i>et al.</i> , "Heterogeneity of Cytokine Secretion Patterns and Functions of Helper T cells," <i>Adv. Immunol.</i> 46:111-147 (1989)	
68	Murray <i>et al.</i> , "Saturation mutagenesis of a major histocompatibility complex protein domain: Identification of a single conserved amino acid important for allorecognition," <i>PNAS USA</i> 85:3535-39 (1988)	
69	Noguchi <i>et al.</i> , "IgE responsiveness to <i>Dermatophagoides farinae</i> in young asthmatic children: IgE binding study using recombinant allergens of Der f1, Der f2 and mutant proteins of Der f2," <i>Int. Arch. Allergy Immunol.</i> 110(4):380-7 (1996)	
70	Ostermeier <i>et al.</i> , "A combinatorial approach to hybrid enzymes independent of DNA homology," <i>Nature</i> 391:1205-09 (1999)	
71	Ostermeier <i>et al.</i> , "Combinatorial protein engineering by incremental truncation," <i>PNAS USA</i> 96:3562-67 (1999)	
72	Parronchi <i>et al.</i> , "IL-4 and IFN (alpha and gamma) exert opposite regulatory effects on the development of cytolytic potential by Th1 or Th2 human T cell clones," <i>J. Immunol.</i> 149(9):2977-83 (1992)	
73	Paul, <i>The Immune System: An Introduction</i> , Chap. 1, pp. 1-20 in FUNDAMENTAL IMMUNOLOGY (W. E. Paul. New York, Raven Press, 1993)	
74	Porcelli, "The CD1 family: a third lineage of antigen-presenting molecules," <i>Adv. Immunol.</i> 59:1-98 (1995)	
Examiner Signature		Date Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

75	Pumpens <i>et al.</i> , "Hepatitis B virus core particles as epitope carriers," <i>Intervirology</i> 38(1-2):63-74 (1995)
76	Quaratino <i>et al.</i> , "Similar antigenic surfaces, rather than sequence homology dictate T-cell epitope molecular mimicry," <i>PNAS USA</i> 92:10398-402 (1995)
77	Randhawa <i>et al.</i> , "In vitro culture of B-lymphocytes derived from Epstein-Barr-virus-associated posttransplant lymphoproliferative disease: cytokine production and effect of interferon-alpha," <i>In Vitro Cell Dev. Biol. Anim.</i> 33(10):803-08 (1997)
78	Sambrook <i>et al.</i> , MOLECULAR CLONING: A LABORATORY MANUAL, Cold Spring Harbor Laboratory Press, New York (2d ed. 1989), Vol. I, pp. 1.53-1.59
79	Sambrook <i>et al.</i> , MOLECULAR CLONING: A LABORATORY MANUAL, Cold Spring Harbor Laboratory Press, New York (2d ed. 1989), Vol. II, pp. 15.51-15.113
80	Schrijver <i>et al.</i> , "Comparison of DNA application methods to reduce BRSV shedding in cattle," <i>Vaccine</i> 16(2-3):130-4 (1998)
81	Simmons <i>et al.</i> , "Potent inhibition of HIV-1 infectivity in macrophages and lymphocytes by a novel CCR5 antagonist," <i>Science</i> 276:276-9 (1997)
82	Stern <i>et al.</i> , Chap. 4, <i>Interleukin-12</i> , in HUMAN CYTOKINES: HANDBOOK FOR BASIC AND CLINICAL RESEARCH 74-96 (Aggarwal & Gutterman eds., 1996)
83	Tan <i>et al.</i> , "Characterization of IL-10 Receptors on Human and Mouse Cells," <i>J. Biol. Chem.</i> 268(28):21053-59 (1993)
84	Thomas <i>et al.</i> , "Potent interleukin 3 receptor agonist with selectively enhanced hematopoietic activity relative to recombinant human interleukin 3," <i>PNAS USA</i> 92:3779-83 (1995)
85	Tuite, "Strategies for the genetic manipulation of <i>Saccharomyces cerevisiae</i> ," <i>Crit. Rev. Biotechnol.</i> 12(1-2):157-88 (1992)
86	Udagawa <i>et al.</i> , "Interleukin-18 (interferon-gamma-inducing factor) is produced by osteoblasts and acts via granulocyte/macrophage colony-stimulating factor and not via interferon-gamma to inhibit osteoclast formation," <i>J. Exp. Med.</i> 185(6):1005-12 (1997)
87	Ulrich <i>et al.</i> , "Chimeric HBV core particles carrying a defined segment of Puumala hantavirus nucleocapsid protein evoke protective immunity in an animal model," <i>Vaccine</i> 16(2-3):272-80 (1998)
88	Villbrandt <i>et al.</i> , "Investigations of the thermostability and function of truncated <i>Thermus aquaticus</i> DNA polymerase fragments," <i>Protein Eng'g</i> 10(11):1281-88 (1997)
89	Weiner <i>et al.</i> , "Immunostimulatory oligodeoxynucleotides containing the CpG motif are effective as immune adjuvants in tumor antigen immunization," <i>PNAS USA</i> 94:10833-7 (1997)
90	Yao <i>et al.</i> , "Human IL-17: A Novel Cytokine Derived from T Cells," <i>J. Immunol.</i> 155(12):5483-86 (1995)
91	York <i>et al.</i> , "Antigen processing and presentation by the class I major histocompatibility complex," <i>Annu. Rev. Immunol.</i> 14:369-96 (1996)
92	Yoshie <i>et al.</i> , "Novel lymphocyte-specific CC chemokines and their receptors," <i>J. Leukocyte Biol.</i> 62(5):634-44 (1997)
93	Zaremba <i>et al.</i> , "Identification of an enhancer agonist cytotoxic T lymphocyte peptide from human carcinoembryonic antigen," <i>Cancer Res.</i> 57(20):4570-77 (1997)

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

**REFERENCES CITED IN APPENDIX C<sup>1</sup>**

Ref. #	Reference	Claim(s)
1*	Alcami <i>et al.</i> , "A soluble receptor for interleukin-1 beta encoded by vaccinia virus: a novel mechanism of virus modulation of the host response to infection," <i>Cell</i> 71(1): 153-67 (1992)	42
2*	Apostolopoulos <i>et al.</i> , "Breast cancer immunotherapy: Current status and future prospects," <i>Immunol. and Cell. Biol.</i> 74: 457-64 (1996)	76
3*	Atamas <i>et al.</i> , "An alternative splice variant of human IL-4, IL-4 delta 2, inhibits IL- 4-stimulated T cell proliferation," <i>J. Immunol.</i> 156(2): 435-41 (1996)	43
4*	Aversa <i>et al.</i> , "SLAM and its role in T cell activation and Th cell responses." <i>Immunol. Cell Biol.</i> 75(2): 202-5 (1997)	31
5*	Bach <i>et al.</i> , "The IFN gamma receptor: a paradigm for cytokine receptor signaling," <i>Annu. Rev. Immunol.</i> 15: 563-91 (1997)	42
6*	Baggioloni <i>et al.</i> , <i>Annu. Rev. Immunol.</i> 15: 675-705, 675 (1997)	12, 14, 41
7*	Baggioloni <i>et al.</i> , <i>Annu. Rev. Immunol.</i> 15:675-705, 676 (1997)	15
8*	Balbas <i>et al.</i> , "Design and Construction of Expression Plasmid Vectors in Escherichia coli," in METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY, Vol. 185, pp. 14-37 (David V. Goeddel ed., Acad. Press, 1991)	49, 62
9*	Basham <i>et al.</i> , "Synergistic antitumor activity with IFN and monoclonal anti-idiotypic for murine B cell lymphoma. Mechanism of action," <i>J. Immunol.</i> 141(8): 2855-60 (1988)	37
10*	Beck <i>et al.</i> , "Analysis of Multiple <i>Plasmodium falciparum</i> Infections in Tanzanian Children during the Phase II Trial of Malaria Vaccine SPf66," <i>J. Inf. Disease</i> 175: 921-26 (1997)	79

---

<sup>1</sup> The references indicated with an asterisk ("\*") are attached with this list. The remaining references were previously submitted in a separate Information Disclosure Statement.



Ref. #	Reference	Claim(s)
11*	Becket <i>et al.</i> , "Characterization of a Prostate Carcinoma Mucin-Like Antigen (PMA)," <i>Int. J. Cancer</i> 62: 703-10 (1995)	76
12*	Bramson <i>et al.</i> , "Construction of a double recombinant adenovirus vector expressing a heterodimeric cytokine: in vitro and in vivo production of biologically active interleukin-12," <i>Hum. Gene Ther.</i> 7(3): 333-42 (1996)	36
13*	Brusselle <i>et al.</i> , "Role of IFN- $\gamma$ in the Inhibition of Allergic Airway Inflammation Caused by IL-12," <i>Am. J. Respir. Cell Mol. Biol.</i> 17: 767-71 (1997)	25, 26
14*	Censini <i>et al.</i> , " <i>cag</i> , a pathogenicity island of <i>Helicobacter pylori</i> , encodes type I-specific and disease-associated virulence factors," <i>PNAS USA</i> 93: 14648-53 (1996)	77
15*	Chen <i>et al.</i> , "Discontinuous epitopes of hepatitis B surface antigen derived from a filamentous phage peptide library," <i>PNAS USA</i> 93(5): 1997-2001 (1996)	23
16*	Chow <i>et al.</i> , "Improvement of Hepatitis B Virus DNA Vaccines by Plasmids Coexpressing Hepatitis B Surface Antigen and Interleukin-2," <i>J. Virol.</i> 71(1): 169-78 (1997)	20
17*	Ciernik <i>et al.</i> , "Induction of Cytotoxic T Lymphocytes and Antitumor Immunity with DNA Vaccines Expressing Single T Cell Epitopes," <i>J. Immunol.</i> 156: 2369-75 (1996)	81, 82
18*	Cohen <i>et al.</i> , "Host factors in the pathogenesis of HIV disease," <i>Immunol. Rev.</i> 159:31-48 (1997)	15
19*	Cortese <i>et al.</i> , "Selection of biologically active peptides by phage display of random peptide libraries," <i>Curr. Opin. Biotechnol.</i> 7(6): 616-21 (1996)	19
20*	Cramer <i>et al.</i> , "DNA Shuffling of a Family of Genes From Diverse Species Accelerates Directed Evolution," <i>Nature</i> 391: 288-91 (1998)	75
21*	Curtis <i>et al.</i> , "Recombinant Soluble Interleukin-11 (IL-11) Receptor alpha Chain Can Act as an IL-11 Antagonist," <i>Blood</i> 90(11): 4403-12 (1997)	42

Application No.: 09/724,869  
Attorney Docket No.: 0155.130US  
(formerly 18097-030310US)  
BDSM Docket No.: 032705-006

Ref. #	Reference	Claim(s)
22	Cwirla <i>et al.</i> , "Peptides on phage: A vast library of peptide for identifying ligands," <i>PNAS USA</i> 87:6378-6382 (1990)	16, 17, 37
23*	Cwirla <i>et al.</i> , "Peptide Agonist of the Thrombopoietin Receptor as Potent as the Natural Cytokine," <i>Science</i> 276: 1696-9 (1997)	12, 16
24*	Dagan <i>et al.</i> , "High level expression and production of recombinant human interleukin analogs," <i>Protein Exp. Purif.</i> 3(4): 290-4 (1992)	59, 60
25*	Devos <i>et al.</i> , "Interleukin-5 and its receptor: a drug target for eosinophilia associated with chronic allergic disease," <i>J. Leukoc. Biol.</i> 57(6): 813-19 (1995)	26
26*	de Vries <i>et al.</i> , <i>Interleukin-4 and Interleukin-13</i> , Chap. 8, in <i>CYTOKINE REGULATION OF HUMORAL IMMUNITY: BASIC AND CLINICAL ASPECTS</i> 195-215 (C. M. Snapper, West Sussex, UK, John Wiley and Sons, 1996)	26
27*	de Vries <i>et al.</i> , "Modulation of the human IgE response," <i>Eur. Respir. J. Suppl.</i> 22: 58s-62s (1996)	26
28*	de Vries <i>et al.</i> , "Novel fundamental approaches to intervening in IgE-mediated allergic diseases," <i>J. Invest. Dermatol.</i> 102(2): 141-4 (1994)	26
29*	De Waal Malefyt <i>et al.</i> , "A Novel Cytokine Belonging to the IL-10 Gene Family Affects Human Monocytes and T Cells," Abstract, 13th European Immunology Meeting, Amsterdam, Netherlands, June 1997, <i>Immunol. Letters</i> 56(1): 211 (1997)	28, 33, 84
30*	Donnelly <i>et al.</i> , "DNA Vaccines," <i>Annu. Rev. Immunol.</i> 15: 617-48, 620 (1997)	8, 20, 21, 22, 49, 51, 52
31*	Dudler <i>et al.</i> , "A Link Between Catalytic Activity, IgE-Independent Mast Cell Activation and Allergenicity of Bee Venom Phospholipase A <sub>2</sub> ," <i>J. Immunol.</i> 155(5): 2605-13 (1995)	46
32	Dunn, "Phage display of proteins," <i>Curr. Opin. Biotechnol.</i> 7(5): 547-53 (1996)	19

Ref. #	Reference	Claim(s)
33*	Eckhart <i>et al.</i> , "Immunogenic presentation of a conserved gp41 epitope of human immunodeficiency virus type 1 on recombinant surface antigen of hepatitis B virus," <i>J. Gen. Virol.</i> 77 (9): 2001-8 (1996)	56, 58
34*	Fomsgaard <i>et al.</i> , "Improved humoral and cellular immune response against the gp120 V3 loop of HIV-1 following genetic immunization with a chimeric DNA vaccine encoding the V3 inserted in the hepatitis B surface antigen," <i>Scand. J. Immunol.</i> 47(4): 289-95 (1998)	56, 58
35*	Foy <i>et al.</i> , "Immune regulation by CD40 and its ligand GP39," <i>Annu. Rev. Immunol.</i> 14: 591-617 (1996)	31
36*	Fromm <i>et al.</i> , "Expression of genes transferred into monocot and dicot plant cells by electroporation," <i>PNAS USA</i> 82(17): 5824-8 (1985)	65, 66
37	Gaczynska <i>et al.</i> , "Proteasome subunits X and Y alter peptidase activities in opposite ways to the interferon-gamma-induced subunits LMP2 and LMP7," <i>J. Biol. Chem.</i> 271(29): 17275-80 (1996)	55
38*	Gauchat <i>et al.</i> , "Regulation of human IgE synthesis: the role of CD4+ and CD8+ T-cells and the inhibitory effects of interferon-alpha," <i>Eur. Respir. J. Suppl.</i> 13: 31s-38s (1991)	26
39*	Goff <i>et al.</i> , "Laboratory Methods: Efficient Saturation Mutagenesis of a Pentapeptide Coding Sequence Using Mixed Oligonucleotides," <i>DNA</i> 6(4):381-388 (1987)	9, 67, 69, 71
40*	Greenfeder <i>et al.</i> , "Insertion of a Structural Domain of Interleukin (IL)-1B Confers Agonist Activity to the IL-1 Receptor Antagonist," <i>J. Biol. Chem.</i> 270(38): 22460-66 (1995)	12, 41
41*	Grewal <i>et al.</i> , "The CD40-CD154 system in anti-infective host defense," <i>Curr. Opin. Immunol.</i> 9(4): 491-7 (1997)	31
42	Groettrup <i>et al.</i> , "The subunits MECL-1 and LMP2 are mutually required for incorporation in the 20S proteasome," <i>PNAS USA</i> 94: 8970-5 (1997)	55

Ref. #	Reference	Claim(s)
43*	Grunig <i>et al.</i> , "Interleukin-10 is a natural suppressor of cytokine production and inflammation in a murine model of allergic bronchopulmonary aspergillosis," <i>J. Exp. Med.</i> 185(6): 1089-99 (1997)	26
44	Han <i>et al.</i> , <i>PNAS USA</i> 92:9747-9751 (1995)	17
45*	Hannum <i>et al.</i> , "Interleukin-1 receptor antagonist activity of a human interleukin-1 inhibitor," <i>Nature</i> 343(6256): 336-40 (1990)	41
46*	Hathcock <i>et al.</i> , "Comparative Analysis of B7-1 and B7-2 Costimulatory Ligands: Expression and Function," <i>J. Exp. Med.</i> 180: 631-40 (1994)	40
47*	Herz <i>et al.</i> , "Molecular approaches to receptors as targets for drug discovery," <i>J. Recept. Signal Transduct. Res.</i> 17(5): 671-776 (1997)	35
48*	Hess <i>et al.</i> , "Superior efficacy of secreted over somatic antigen display in recombinant <i>Salmonella</i> vaccine induced protection against listeriosis," <i>PNAS USA</i> 93: 1458-63 (1996)	77
49*	Hill <i>et al.</i> , "Mutagenesis with Degenerate Oligonucleotides: An Efficient Method for Saturating a Defined DNA Region with Base Pair Substitutions," in <i>METHODS IN ENZYMOLOGY: RECOMBINANT DNA</i> 155: 558-568 (Ray Wu ed., Acad. Press, Inc., 1987)	9, 67, 69, 71
50*	Horuk, <i>TIPS</i> 15: 159-165, 159 (1994)	14
51*	Horwitz <i>et al.</i> , in <i>METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY</i> 185: 599-611 (David V. Goeddel ed., Acad. Press, Inc. 1990)	9
52*	HUMAN CYTOKINES: HANDBOOK FOR BASIC AND CLINICAL RESEARCH, Vol. II (Aggarwal & Gutterman eds. 1996)	14
53*	HUMAN CYTOKINES: HANDBOOK FOR BASIC AND CLINICAL RESEARCH, Vols. I-II (Aggarwal & Gutterman eds. 1996)	33, 39, 83, 84
54*	Ihle <i>et al.</i> , "Signaling through the hematopoietic cytokine receptors," <i>Annu. Rev. Immunol.</i> 13: 369-98 (1995)	34

Ref. #	Reference	Claim(s)
55	Jiang <i>et al.</i> , "Subtraction hybridization identifies a novel melanoma differentiation associated gene, mda-7, modulated during human melanoma differentiation, growth and progression," <i>Oncogene</i> 11(12): 2477-86 (1995)	28, 33, 84
56*	Kaufman, "Vectors Used for Expression in Mammalian Cells," in METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY, Vol. 185, pp. 487-511 (David V. Goeddel ed., Acad. Press, 1991)	49, 63
57*	Kay <i>et al.</i> , PHAGE DISPLAY OF PEPTIDES AND PROTEINS: A LABORATORY MANUAL (Academic Press 1996)	18, 37
58	Kim <i>et al.</i> , "In Vivo Engineering of a Cellular Response by Coadministration of IL-12 Expression Vector with a DNA immunogen," <i>J. Immunol.</i> 158(2):816-26 (1997)	8, 36
59	Klinman <i>et al.</i> , "Contribution of CpG Motifs to the Immunogenicity of DNA Vaccines," <i>J. Immunol.</i> 158(8): 3635-39 (1997)	24
60*	Krieger <i>et al.</i> , "Structures and functions of multiligand lipoprotein receptors: macrophage scavenger receptors and LDL receptor-related protein (LRP)," <i>Annu. Rev. Biochem.</i> 63: 601-37 (1994)	13
61*	Kroemer <i>et al.</i> , "Immunoregulation by cytokines," <i>Crit. Rev. Immunol.</i> 13(2): 163-91 (1993)	32, 34
62*	Laberge <i>et al.</i> , <i>J. Immunol.</i> 156(1): 310-5 (1996)	33, 84
63*	Le Borgne <i>et al.</i> , "In Vivo Induction of Specific Cytotoxic T Lymphocytes in Mice and Rhesus Macaques Immunized with DNA Vector Encoding an HIV Epitope Fused with Hepatitis B Surface Antigen," <i>Virology</i> 240: 304-15 (1998)	56, 58
64*	Le Grice, "Regulated Promoter for High-Level Expression of Heterologous Genes for <i>Bacillus subtilis</i> ," in METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY, Vol. 185, pp. 201-214 (David V. Goeddel ed., Acad. Press, 1991)	49, 62
65*	Levinson, "Expression of Heterologous Genes in Mammalian Cells," in METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY, Vol. 185, pp. 485-4871 (David V. Goeddel ed., Acad. Press, 1991)	49, 63

Ref. #	Reference	Claim(s)
66*	Livnah <i>et al.</i> , "Functional Mimicry of a Protein Hormone by a Peptide Agonist: The EPO Receptor Complex at 2.8 ," <i>Science</i> 273: 464-71 (1996)	12, 16
67*	Ma <i>et al.</i> , "Antibody production and engineering in plants," <i>Ann. NY Acad. Sci.</i> 792: 72-81 (1996)	64
68*	Mattion <i>et al.</i> , "Characterization of recombinant polioviruses expressing regions of rotavirus VP4, hepatitis B surface antigen, and herpes simplex virus type 2 glycoprotein D," <i>J. Virol.</i> 69: 5132-37 (1995)	78
69*	McLafferty <i>et al.</i> , "M13 bacteriophage displaying disulfide-constrained microproteins," <i>Gene</i> 128(1): 29-36 (1993)	19
70*	Miele, "Plants as bioreactors for biopharmaceuticals: regulatory considerations," <i>Trends Biotechnol.</i> 15(2): 45-50 (1997)	64
71*	Mosmann <i>et al.</i> , "Heterogeneity of Cytokine Secretion Patterns and Functions of Helper T cells," <i>Adv. Immunol.</i> 46: 111-147 (1989)	38, 44, 45
72*	Murray <i>et al.</i> , "Saturation mutagenesis of a major histocompatibility complex protein domain: Identification of a single conserved amino acid important for allorecognition," <i>PNAS USA</i> 85:3535-39 (1988)	9, 67, 69, 71
73*	Noguchi <i>et al.</i> , "IgE responsiveness to <i>Dermatophagoides farinae</i> in young asthmatic children: IgE binding study using recombinant allergens of Der f1, Der f2 and mutant proteins of Der f2," <i>Int. Arch. Allergy Immunol.</i> 110(4): 380-7 (1996)	46
74*	Ostermeier <i>et al.</i> , "Combinatorial protein engineering by incremental truncation," <i>PNAS USA</i> 96: 3562-67 (1999)	73
75*	Ostermeier <i>et al.</i> , "A combinatorial approach to hybrid enzymes independent of DNA homology," <i>Nature</i> 391: 1205-09 (1999)	73
76*	Parronchi <i>et al.</i> , "IL-4 and IFN ( $\alpha$ and $\gamma$ ) exert opposite regulatory effects on the development of cytolytic potential by Th1 or Th2 human T cell clones," <i>J. Immunol.</i> 149(9): 2977-83 (1992)	26, 38, 39

Ref. #	Reference	Claim(s)
77	Paul <i>et al.</i> , "Lymphocyte responses and cytokines," <i>Cell</i> 76: 241-251, 241-242 (1994)	12, 14, 38, 39, 41, 44, 45, 83
78*	Paul, <i>The Immune System: An Introduction</i> , Chap. 1, pp. 1-20 in FUNDAMENTAL IMMUNOLOGY (W. E. Paul. New York, Raven Press, 1993)	81, 82
79	Pisetsky, "Immune Activation by Bacterial DNA: A New Genetic Code," <i>Immunity</i> 5: 303-10 (1996)	24
80*	Porcelli, "The CD1 family: a third lineage of antigen-presenting molecules," <i>Adv. Immunol.</i> 59: 1-98 (1995)	31
81*	Premack <i>et al.</i> , <i>Nature Med.</i> 2(11): 1174-1178, 1174 (1996)	14
82*	Pumpens <i>et al.</i> , "Hepatitis B virus core particles as epitope carriers," <i>Intervirology</i> 38(1-2): 63-74 (1995)	22
83*	Quaratino <i>et al.</i> , "Similar antigenic surfaces, rather than sequence homology dictate T-cell epitope molecular mimicry," <i>PNAS USA</i> 92: 10398-402 (1995)	80
84*	Randhawa <i>et al.</i> , "In vitro culture of B-lymphocytes derived from Epstein-Barr-virus-associated posttransplant lymphoproliferative disease: cytokine production and effect of interferon-alpha," <i>In Vitro Cell Dev Biol Anim.</i> 33(10): 803-8 (1997)	37
85*	Sambrook <i>et al.</i> , MOLECULAR CLONING: A LABORATORY MANUAL, Cold Spring Harbor Laboratory Press, New York (2d ed. 1989)	46, 47, 54, 74, 85, 86
86*	Sambrook <i>et al.</i> , MOLECULAR CLONING: A LABORATORY MANUAL, Cold Spring Harbor Laboratory Press, New York (2d ed. 1989), pp. 1.53-1.59	7
87*	Sambrook <i>et al.</i> , MOLECULAR CLONING: A LABORATORY MANUAL Cold Spring Harbor Laboratory Press, New York (2d ed. 1989) pp. 15.51-15.113	9

Ref. #	Reference	Claim(s)
88	Sayers <i>et al.</i> , "5'-3' Exonucleases in phosphorothioate-based oligonucleotide-directed mutagenesis," <i>Nucleic Acids Res.</i> 16: 791-802 (1988)	73
89*	Schrijver <i>et al.</i> , "Comparison of DNA application methods to reduce BRSV shedding in cattle," <i>Vaccine</i> 16(2-3): 130-4 (1998)	52
90*	Simmons <i>et al.</i> , "Potent inhibition of HIV-1 infectivity in macrophages and lymphocytes by a novel CCR5 antagonist," <i>Science</i> 276 (5310):276-9 (1997)	15
91	Stemmer, "Searching Sequence Space," <i>Biotechnology</i> 13: 549-53 (1995)	75
92*	Stern <i>et al.</i> , Chap. 4, <i>Interleukin-12</i> , in HUMAN CYTOKINES. HANDBOOK FOR BASIC AND CLINICAL RESEARCH 74-96 (Aggarwal & Gutterman eds., 1996)	26
93	Stohwasser <i>et al.</i> , "Molecular cloning of the mouse proteasome subunits MC14 and MECL-1: reciprocally regulated tissue expression of interferon-gamma-modulated proteasome subunits," <i>Eur. J. Immunol.</i> 27(5): 1182-7 (1997)	55
94*	Tan <i>et al.</i> , "Characterization of recombinant extracellular domain of human interleukin-10 receptor." <i>J. Biol. Chem.</i> 270(21): 12906-11 (1995)	27, 28, 43
95	Tan <i>et al.</i> , "Characterization of IL-10 Receptors on Human and Mouse Cells," <i>J. Biol. Chem.</i> 268(28): 21053-59 (1993)	27
96*	Thomas <i>et al.</i> , "Potent interleukin 3 receptor agonist with selectively enhanced hematopoietic activity relative to recombinant human interleukin 3," <i>PNAS USA</i> 92: 3779-83 (1995)	12
97*	Tuite, "Strategies for the genetic manipulation of <i>Saccharomyces cerevisiae</i> ," <i>Crit. Rev. Biotechnol.</i> 12(1-2): 157-88 (1992)	63
98*	U.S. Pat. No. 6,376,246	68, 69, 70, 72
99	U.S. Pat. No. 5,571,698, col. 48, ll. 45-65	19



Application No.: 09/724,869  
Attorney Docket No.: 0155.130US  
(formerly 18097-030310US)  
BDSM Docket No.: 032705-006

Ref. #	Reference	Claim(s)
100	U.S. Pat. No. 5,571,698, col. 7, ll. 37-38 and col. 47, l. 65 to col. 48, l. 22	18
101	U.S. Pat. No. 5,571,698	17
102	U.S. Pat. No. 5,348,867	18
103*	Udagawa <i>et al.</i> , "Interleukin-18 (interferon-gamma-inducing factor) is produced by osteoblasts and acts via granulocyte/macrophage colony-stimulating factor and not via interferon-gamma to inhibit osteoclast formation," <i>J. Exp. Med.</i> 185(6): 1005-12 (1997)	33, 84
104*	Ulrich <i>et al.</i> , "Chimeric HBV core particles carrying a defined segment of Puumala hantavirus nucleocapsid protein evoke protective immunity in an animal model," <i>Vaccine</i> 16(2-3): 272-80 (1998)	22
105*	Villbrandt <i>et al.</i> , <i>Protein Eng'g</i> 10(11): 1281-88 (1997)	50
106*	Weiner <i>et al.</i> , "Immunostimulatory oligodeoxynucleotides containing the CpG motif are effective as immune adjuvants in tumor antigen immunization," <i>PNAS USA</i> 94: 10833-7 (1997)	24
107	WEIR'S HANDBOOK OF EXPERIMENTAL IMMUNOLOGY (Leonore A. Herzenberg <i>et al.</i> eds., 5 <sup>th</sup> ed. 1996)	85, 86
108	WO 99/41383	48, 50
109	WO 99/41369	49, 50
110	WO 99/41368	9-11
111	WO 99/23107	48, 50, 73
112	WO 98/27230	9-11, 48, 50, 74
113*	WO 94/18330	17
114*	WO 94/01567	17
115*	WO 92/18619	19

Application No.: 09/724,869  
Attorney Docket No.: 0155.130US  
(formerly 18097-030310US)  
BDSM Docket No.: 032705-006

Ref. #	Reference	Claim(s)
116	WO 92/06204	19
117*	WO 92/01047	19
118*	WO 91/19818	19
119*	Yao <i>et al.</i> , "Human IL-17: A Novel Cytokine Derived from T Cells," <i>J. Immunol.</i> 155(12): 5483-6 1995	33, 84
120*	York <i>et al.</i> , "Antigen processing and presentation by the class I major histocompatibility complex," <i>Annu. Rev. Immunol.</i> 14: 369-96 (1996)	55, 56
121*	Yoshie <i>et al.</i> , "Novel lymphocyte-specific CC chemokines and their receptors," <i>J. Leukoc. Biol.</i> 62(5): 634-44 (1997)	15, 65, 66
122*	Zaremba <i>et al.</i> , "Identification of an enhancer agonist cytotoxic T lymphocyte peptide from human carcinoembryonic antigen," <i>Cancer Res.</i> 57(20): 4570-7 (1997)	58, 80